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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,405	11/21/2001	Alan L. Mueller	50877.0030	4028

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EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	**PAPER NUMBER**
1614	
MAIL DATE	**DELIVERY MODE**
05/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/990,405	MUELLER ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,6 and 21-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,6 and 21-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Applicant's argument and Declaration, filed 02/12/07, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

2. Claims 5-6 and 21-34 are currently pending for prosecution on the merits

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

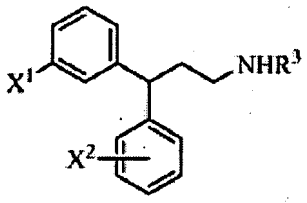
The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

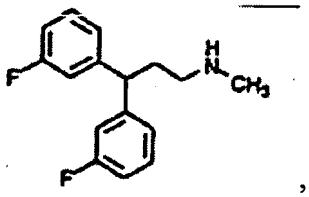
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

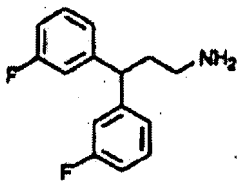
the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

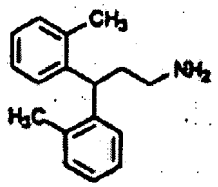
3. Claims 5-6 and 21-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mueller et al. (WO 96/40097) in view of Skolnick et al. (Pharmacopsychiatry, abstract, 1996 January, 29:1, 23-6).

The claims read on a method of treating a patient for depression comprising a compound of the formula 

. Further limitation includes "X^1 is -F, -Cl, $-OCF_3$ or $-CF_3$ and X^2 is either $2\text{-}OCH_3$, $2\text{-}CH_3$, 3-F, $3\text{-}CF_3$, or $4\text{-}CF_3$" (claim 6); "X^1 and X^2 are -F, and R^3 is –H" (claim 21); "X^2 is at the 3-position" (claim 22); "X^1 and X^2 are -F, and R^3 is -CH3" (claim 23); "X^2 is at the 3-position" (claim 24); "the compound is active at a serotonin reuptake site and at a N-methyl-D-aspartate (NMDA) receptor" (claim 25); "the compound has an NMDA receptor IC_{50} of about 50 nM to about 1 μM" (claim 26), "the compound has an NMDA receptor of IC_{50} of about 100 nM to about 800 nM" (claim 27); and the compound of



, 

, 

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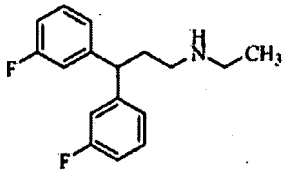
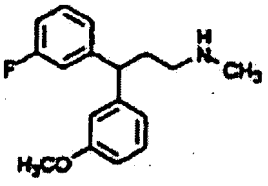
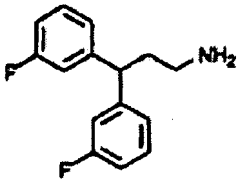
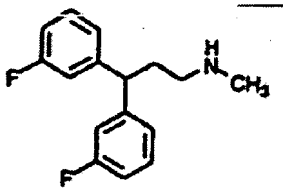
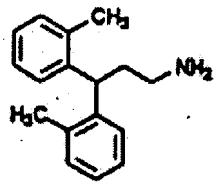
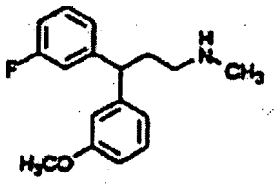
 or  (claims 28-35) or pharmaceutically acceptable salts.

Mueller teaches arylalkylamine compounds represented by the formula or their pharmaceutically acceptable salt as a potent NMDA receptor antagonist, for example

 (compound 20) having NMDA receptor IC_{50} of 0.070 μM (equivalent to 70 nM),  (compound 60) having NMDA receptor IC_{50} of 0.416 μM (equivalent to 416 nM),  (compound 65) having NMDA receptor IC_{50} of 0.167 μM (equivalent to 167 nM) and  (compound 142), that is useful for the treatment of neurological disorders including epilepsy, Alzheimer's disease, Parkinson's disease, and Huntington's disease (abstract; pages 24-25; pages 62-64; page 255, line 16 thru page 256, line 9; claims 1, 18, 19 and 77 and 80; Table 5-7 and 9). Mueller also discloses that

said arylallylamine compounds do not have PCP-like psychotomimetic activity (page 122, lines 9-12; page 32, lines 3-10; page 96, lines 8-22) and have an $IC_{50} \leq 10\mu M$ at NMDA receptor, more preferably $\leq 2.5\mu M$, and most preferably $\leq 0.5\mu M$ (equivalent to 500 nM) at an NMDA receptor (page 50, lines 28-24 and claims 73-75); and shows activity at a serotonin reuptakes site and at a N-methyl-D-aspartate (NMDA) receptor (Table 10).

Skolnick provides links between NMDA receptor antagonist and the treatment of depression. Skolnick teaches that NMDA antagonist mimic the effects of clinically effective antidepressants in both preclinical tests predictive antidepressant action and procedures designed to model aspects of depressive symptomatology; and NMDA receptors is involved in the pathophysiology of depression (abstract).

The teaching of Mueller differs from the claimed invention in the use of the claimed compounds represented by the formula, namely the compound 20, 25, 60 and 142, for the treatment of depression. To incorporate such teaching into the teaching of Mueller, would have been obvious in view of Skolnick who teaches nexus between NMDA receptor antagonist and the treatment of depression.

One having ordinary skilled in the art at the time of the invention was made would have expected as taught by Skolnick that NMDA receptor mechanism is involved in pathophysiology of depression and the downregulation of NMDA receptor by NMDA antagonist would provide clinical utility in the treatment of depression. One having ordinary skill in the art would have been motivated to make the modification such that the adverse effect associated with inhibition of NMDA receptor mediated response (e.g., PCP-like psychotomimetic effect) would be greatly decreased by the administration of the claimed compound. One would have been motivated to

combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

With respect to the "the compound is active at a serotonin reuptake site and at a N-methyl-D-aspartate (NMDA) receptor" (claim 25), "the compound has an NMDA receptor IC_{50} of about 50 nM to about 1 μM" (claim 26) and "the compound has an NMDA receptor of IC_{50} of about 100 nM to about 800 nM" (claim 27), as discussed in preceding comments, those characteristics or properties are deemed to be present in the referenced arylalkylamine analogs such as compound 20, 25, 60 and 142. Thus, the above references in combination makes obvious the instant invention.

Relevant Prior Art of Record

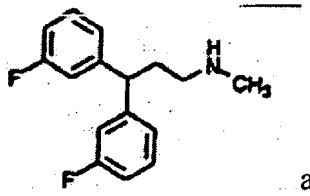
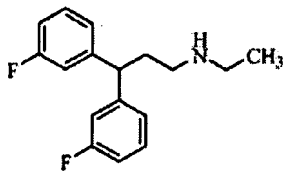
4. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure. Please reference Jones et al. (Journal of Medicinal Chemistry, 1971, Vol. 14, No. 2, pp. 161-164).

Response to Arguments

5. As stated above, applicant's arguments and Declaration filed 02/12/07 have been fully considered but they are not persuasive.

Applicant's argument takes the position that Skolnic does not provide sufficient to data to provide a reasonable expectation that all NMDA receptor antagonists would treat depression; and empirical data indicates that many NMDA receptor antagonist do not possess antidepressant activity. Applicant alleges that based on the limited data of Skolnick and the contrary submitted

empirical data, the skill artisan would not have reasonable expectation that any particular NMDA receptor antagonist to exhibit antidepressant activity.

This argument is not found persuasive. Unlike the applicant's argument, at the time of the invention was made, one of ordinary skill in the art would have understood (as evidenced by Jones et al. (Journal of Medicinal Chemistry, 1971, Vol. 14, No. 2, pp. 161-164)) that the compounds of Mueller'097 would have similar activity as Jones due to close (or same) structural similarity of the compounds (in fact the instantly claimed  and  are disclosed as potential antidepressant agent in Table 3). Therefore, one having ordinary skill in the art would have motivated to combine Mueller and Skolnick with the reasonable expectation of success that the claimed compounds having NMDA antagonist property would treat depression.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. No Claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Brian Kwon
Primary Patent Examiner
AU 1614